

Spot urine cortisol–creatinine ratio – A useful screening test in the diagnosis of Cushing's syndrome

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ABSTRACT

Introduction: Although, there are several tests available, not one of them fulfils the criteria of being an ideal screening test. Continuing the search for an ideal screening test, we explored the use of urine spot cortisol-creatinine ratio as a novel method of evaluating patients with Cushing's syndrome. **Method:** A total of 35 subjects were studied and divided into 3 groups - 15 having Cushing's syndrome, 15 patients with obesity and 5 normal weight subjects. All patients with Cushing's syndrome were positive for the other screening tests. **Results:** The mean (standard deviation) of cortisol:creatinine ratio among the 3 groups (Cushing's, obese and control subjects) was 36.00(24.74), 7.01(2.73) and 3.49(2.68) respectively. Using the cutoff of 12.27 nano mol/ micro mol (based on data of normal subjects) for the urine cortisol creatinine ratio we get a sensitivity of 93.75% and a specificity of 100%. Also the positive and negative predictive value as calculated with this cutoff is 100% and 93.3% respectively. **Conclusion:** In this study we found that UCCR is similar in both Obese and Non Obese subjects who did not have Cushing's syndrome. UCCR is significantly elevated in individuals with Cushing's syndrome as compared to those who do not have Cushing's syndrome. Also when a cut off of 12.27 nano mol/ micro mol was used this test had a higher sensitivity, however this test had a higher specificity at a cut off of 15.35.

Key words: Urine Cortisol creatinine ratio, Cushing's syndrome, endogenous

INTRODUCTION

Endogenous Cushing's syndrome has an increasing prevalence over the last few years. If left undiagnosed, it is associated with a high morbidity and mortality. Despite being a rare entity, it is often suspected among patients with new onset, unexplained, difficult to treat diabetes, hypertension, and osteoporosis.^[1] All these factors warrant this disease to have a good screening test.

At present, the screening tests of Cushing's syndrome are based on the demonstration of increased cortisol

production in blood and urine. Even though, there are several tests available, not one of them fulfils the criteria of being an ideal screening test. Continuing the search for an ideal screening test, we explored the use of urine spot cortisol–creatinine ratio^[2] as a novel method of evaluating patients with Cushing's syndrome.

The amount of cortisol in the urine reflects the average cortisol concentration in the blood at the time when that the urine was formed. However, this measurement is affected by the concentration of the urine. Creatinine, a product of muscle metabolism, is normally lost in the urine at a relatively steady rate. Because of this, the ratio of cortisol:creatinine in the urine can be used to determine for the effect of urine concentration.

Performing a urine

Cortisol:creatinine ratio as a screening test will be a non-invasive, rapid, and inexpensive test, which can be done on an outpatient basis.

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Aims and objectives

In this study, we had the following objectives:

1. To assess the efficacy of urine spot cortisol:creatinine ratio as a novel tool for screening patients with Cushing's syndrome as compared to other existing diagnostic tests for Cushing's syndrome.
2. To compare this test in normal subjects, obese subjects, and patients with Cushing's syndrome.

MATERIALS AND METHODS

This was a cross-sectional prospective study, where in data was collected from the participants at one point while subjecting them to the routine screening tests for endogenous Cushing's syndrome. All patients with suspected endogenous Cushing's syndrome, attending our Hospital, were reviewed over a period of 1 year (2011-2012).

A morning urine sample was obtained for detecting the spot cortisol:creatinine ratio. This study was approved by the Institutional review board prior to initiation. We included all subjects with clinical and biochemical evidence of endogenous Cushing's syndrome, having a normal renal function. We excluded patients with exogenous Cushing's syndrome.

RESULTS

A total of 35 subjects were studied and divided into three groups—15 having Cushing's syndrome, 15 patients with obesity, and 5 normal weight subjects. All patients, with Cushing's syndrome were positive for the other screening tests. Among patients with Cushing's syndrome 7 had Cushing's disease, 5 had an adrenal adenoma, 2 had an ectopic adrenocorticotrophic hormone (ACTH) producing tumor, and 1 had an adrenal cell carcinoma.

The mean (standard deviation) of cortisol:creatinine ratio among the three groups (Cushing's, obese, and control subjects) was 36.00 (24.74), 7.01 (2.73), and 3.49 (2.68), respectively. The mean ratio between the obese and control groups were grouped under the same category as non-

Cushing's syndrome. The mean (standard deviation) of cortisol:creatinine ratio between patients with Cushing's syndrome and non-Cushing's patients was 36.00 (24.74) and 6.13 (3.07). These values were statistically significant ($P \leq 0.001$).

Using the cut-off of 12.27 nmol/ μ mol (based on data of normal subjects) for the urine cortisol creatinine ratio we get a sensitivity of 93.75% and a specificity of 100%. Also the positive and negative predictive value as calculated with this cut-off is 100% and 93.3%, respectively.

However, if we use the cut-off of 15.35 nmol/ μ mol (based on reference 6) for the urine cortisol creatinine ratio we get a sensitivity of 86.6% and a specificity of 100%. Also the positive and negative predictive value as calculated with this cut-off is 100% and 93.75%, respectively.

CONCLUSION

In this study, we found that urine cortisol creatinine ratio (UCCR) is similar in both obese and non-obese subjects, who did not have Cushing's syndrome. UCCR is significantly elevated in individuals with Cushing's syndrome, as compared to those who do not have Cushing's syndrome. Also, when a cut-off of 12.27 nmol/ μ mol was used this test had a higher sensitivity, however, this test had a higher specificity at a cut-off of 15.35.

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